REMARKS

As a result of the foregoing amendments, claims 2 and 8-10 have been amended to correct typographical or antecedent errors and claims 6 and 7 have been amended to correct their dependency from claims 5 and 6, respectively, to claim 2. No new matter has been entered by these amendments. Entry of these amendments and reconsideration of pending claims 1-10, 20, 21 and 25 are respectfully requested.

§112 Rejection of Claim 2 Overcome by Amendment

Reconsideration and withdrawal of the rejection of claim 2 as indefinite under 35 U.S.C. §112, second paragraph, are respectfully requested. In the amendment filed December 29, 2003, typographical errors occurred in the listing of Claim 2. Claim 2 has been amended above, to return it to the form of the original filing of this application. As a result of this amendment, the claim no longer contains the term "TOM" which was the cause of this indefiniteness rejection. Accordingly, this rejection has been overcome and should be withdrawn.

§103 Rejection of Claims 1-3, 20 and 21 Over Gaber In View of Ketchum and Fairman is Improper for Lack of Reasonable Expectation of Success in Proposed Combination of Art

Reconsideration and withdrawal of the rejection of claims 1-3, 20 and 21 under 35 U.S.C. §103(a), as being unpatentable over the combination of US 5,795,770 (Graber) in view of Ketchum et al. and Fairman et al., are respectfully requested. According to the rejection, all the limitations of the rejected claims are taught or suggested by the combination of prior art because:

Graber teaches assays for identifying inhibitors or activators of eukaryotic potassium channels expressed in mutant *S. cerevisiae* cells having inactivated endogenous potassium channels TRK1 and TRK2;

Ketchum et al teaches the existence of a third endogenous potassium channel in *S. cerevisiae*, TOK1;

Fairman et al teaches a triple deletion mutant of *S. cerevisiae*, in which TRK1, TRK2 and TOK1 are inactivated, and this triple deletion "...grows less well than does the double knockout, trk1Δ, trk2Δ..." (sentence bridging pages 153 and 154) ; and

one of skill in the art would have been motivated to use the triple deletion mutant of Fairman et al in the complementation assays of Graber due to an expectation that this would increase the sensitivity of the complementation assay by the deletion of the third and final endogenous potassium channel from that yeast cell.

Applicants respectfully submit that this rationale, and the rejection based on it, are improper, because one of skill in this art would *not* have a reasonable expectation of success in using the triple deletion mutant of Fairman et al in place of the double deletion mutant of the complementation assays of Graber.

"The prior art can be modified or combined to reject claims as *prima facie* obvious as long as there is a reasonable expectation of success." *In re Merck & Co., Inc.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986), cited at MPEP 2143.02. Applicants respectfully submit that one of skill in the art, with full knowledge of Graber, Ketchum et al and Fairman et al, would not have had a reasonable expectation of success in using the triple deletion mutants of Fairman et al as a substitute for the double deletion mutants in the Graber complementation assay. As is well known in the art, a complementation assay, such as that taught by Graber, functions when the heterologous gene added to the yeast serves to replace, or at least alleviate, the loss of function due to inactivation of endogenous genes in the yeast. As the pathology associated with the inactivation of endogenous genes becomes more severe, complementation assays become more difficult. In essence, as the pathology caused by inactivation of endogenous yeast genes increases, it becomes less and less likely that the heterologous gene added to the yeast for a complementation assay can sufficiently reverse that pathology to produce meaningful assay results.

One of skill in the art, knowing the teaching of Graber (that at least one heterologous eukaryotic potassium ion channel, KAT1, can serve in a yeast cell to move enough potassium ions to successfully complement a yeast mutant missing two endogenous potassium ion channels, TRK1 and TRK2), would have no way of predicting whether KAT1, or any other eukaryotic potassium ion channel, would be capable of moving enough potassium ions into a yeast cell to successfully complement a yeast cell that was modified to inactivate ***all three*** endogenous potassium ion channels, TRK1, TRK2 and TOK1. This is particularly true where the prior art already teaches that the triple deletion mutant (trk1Δ, trk2Δ, tok1Δ) has a more pronounced pathology than the double deletion mutant (trk1Δ, trk2Δ). See Fairman, et al, in the paragraph bridging pages 153 and 154. Applicants respectfully submit that where it is impossible for one of skill in the art to predict success or failure, there is no reasonable expectation of success.

§103 Rejection of Claims 1-10, 20, 21 and 25 Over Gaber In View of Ketchum and Fairman and further in view of Tang and Rampe is Improper for Lack of Reasonable Expectation of Success in Proposed Combination of Art

Reconsideration and withdrawal of the rejection of claims 1-10, 20, 21 and 25 under 35 U.S.C. §103(a), as being unpatentable over the combination of Graber in view of Ketchum et al. and Fairman et al. and further in view of Tang and Rampe, are respectfully requested. This rejection relies on the same motivation as the rejection over the combination of Graber, Ketchum et al and Fairman et al, above. Accordingly, this rejection suffers from the same lack of a reasonable expectation of success and is improper. The addition of Tang and Rampe to the combination provide no guidance, whatsoever, that would enable one of skill in the art to predict whether eukaryotic potassium ion channels which can complement the loss of two endogenous potassium ion channels in a yeast (Gaber) can also complement the more severe pathology of the deletion of all three endogenous potassium ion channels in a yeast, as required by the instant claims.

Applicants respectfully submit that the application is now in condition for allowance and request prompt notice thereof.

Respectfully submitted,

F. Aaron Dubberley, Reg. No., 41,001
Attorney/Agent for Applicant

Aventis Pharmaceuticals Inc.
Patent Department
Route #202-206 / P.O. Box 6800
Bridgewater, NJ 08807-0800
Telephone (908) 231-3737
Telefax (908) 231-2626

Aventis Docket No. DEAV2000/A002 US NP